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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/169,048	10/08/1998	WILLIAM D. HUSE	P-IX-3280	5187

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MCDERMOTT, WILL & EMERY
4370 LA JOLLA VILLAGE DRIVE, SUITE 700
SAN DIEGO, CA 92122

EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 03/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/169,048	HUSE ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10-45* is/are pending in the application.

4a) Of the above claim(s) *19-38,42,44 and 45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-18,39-41 and 43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 10-45 are pending. Claims 19-38, 42, 44 and 45 are withdrawn from consideration. Claims 10-18 and 39-41, and 43 are examined.

Continued Examination Under 37 CFR 1.114

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/2/2004 has been entered.

Election/Restrictions

3. The Requirement for Restriction/Election, mailed 2/28/2000, and as considered in the Office action mailed 11/22/2000, is maintained. Applicant's election with traverse of Group II, original claims 10-18, filed 9/5/2000, is acknowledged.

4. Claims 19-38 remain withdrawn from consideration as drawn to a non-elected invention. Claims 42, 44 and 45 remain withdrawn from consideration as drawn to a non-elected species, there being no allowable generic claim.

Priority

5. This application claims benefit of Provisional Application 60/112,011, filed 10/9/1997. This application is related to pending divisional application 09/839,469.

Specification

Applicant is reminded of the proper language and format for an abstract of the disclosure.

The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited. The form and legal phraseology often used in patent claims, such as "means" and "said," should be avoided. The abstract should describe the disclosure sufficiently to assist readers in deciding whether there is a need for consulting the full patent text for details.

The language should be clear and concise and should not repeat information given in the title. It should avoid using phrases which can be implied, such as, "The disclosure concerns," "The disclosure defined by this invention," "The disclosure describes," etc.

6. The abstract apparently exceeds 150 words. Correction is necessary.

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The specification does not describe recombinantly expressing a ligand variant population in melanophores, as in claim 16.

Withdrawn Rejections

8. The rejection of claims 10-18, 40, 41 and 43, under 35 U.S.C. 112, first paragraph, for claiming new matter is withdrawn in view of applicant's arguments.

9. The rejection of claims 10-18, 40, 41 and 43 under 35 U.S.C. 112, first paragraph, for lack of enablement, is withdrawn in view of applicant's arguments.

10. The rejections of claims 10, 17, 39 and 40, under 35 U.S.C. 112, second paragraph, are withdrawn in view of applicant's arguments and amendments.

11. The rejection of claim 41, under 35 U.S.C. 102(b), is withdrawn in view of applicant's arguments.

12. The rejections of claims 10-14, 17, 18 40 and 43, under 35 U.S.C. 103, is withdrawn in view of applicant's arguments.

Maintained Rejections

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

13. Claims 10-18 and 39-41, and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection. This rejection maintains and supersedes the rejection for lacking written description, as set forth in the previous Office action.

Briefly, the instant claims recite a method for determining binding of a ligand to a receptor comprising contacting a collective ligand variant population with a population of receptors and detecting binding of a receptor from said population of receptors to a ligand from said collective ligand variant population.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention claimed.

The instant specification discloses that a 'receptor' is capable of selectively binding to a ligand, and is, generally, a macromolecule, such as a polypeptide, a nucleic acids, carbohydrate or lipid; 'ligand' refers to a molecule selectively bind to a receptor, and the ligand can be any type of molecule such as a polypeptide, nucleic acid, carbohydrate, lipid or any organic derived compound; and the further the specification

discloses that a ligand can be a receptor and conversely, a molecule that is a receptor can also be a ligand, because ligands and receptors are defined as binding partners. The specification discloses that a 'variant' is a molecule that shares **similar** structure and function; and 'optimal binding' characteristics will depend on the particular application of the binding molecule.

The specification example discloses that the parent receptor is a mouse monoclonal antibody, and six variant receptors were generated and screened for binding to anti-idiotypic antibody ligands. The specification has no other examples of ligands, receptors or variants of receptors. The specification has not disclosed methods in which the receptor variant population is divided into subpopulations. The specification discloses hypothetical methods, in which the receptor population can be screened by dividing ligand populations into subpopulations or individual ligands, in order to determine the binding activity (see specification at p. 6, line 18-p. 7, line 3). The specification discloses general methods for expressing the receptor variants in melanophore cells (Example I).

The specification has not disclosed any particular oligonucleotide or carbohydrate or lipid or organic molecule as 'ligand' or 'receptor.' The specification has not disclosed the receptor variant which binds to a ligand identified by the claimed method. The specification discloses general methods of identifying a receptor sequence which specifically binds to a ligand, and methods of generating variants of the receptor recombinantly, and methods of screening for the variant ligand. The

specification does not describe recombinantly expressing a *ligand* variant population in melanophores.

With regard to the description requirement, Applicants' attention is invited to decisions of the Court of Appeals for the Federal Circuit, which has held that a written description of an invention involving a chemical genus, like a description of a chemical species, requires a precise definition, such as by structure, formula [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials. *University of California v. Eli Lilly and Co.,* 43 USPQ2d 1398, 1405 (1997), quoting *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) (bracketed material in original) [The claims at issue in *University of California v. Eli Lilly* defined the invention by function of the claimed DNA (encoding insulin)]. Thus, it requires a representative sample of compounds (i.e., receptor, ligand) or a showing of sufficient characteristics to demonstrate possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention (see MPEP 2163).

The instant specification discloses general hypothetical methods in which binding partners can be identified. The specification has no working examples other than the mouse monoclonal antibody variants and anti-idiotypic antibody which binds to it as ligands and receptors.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently detailed to show that applicant was in possession of the claimed invention as a whole. See, e.g., Vas-Cath, 935 F.2d at 1565, 19 USPQ2d at 1118. In the present instance, the claimed invention contains no identifying characteristics regarding the receptors, ligands or the receptor variant, except the generic definitions. The variant receptors have to be prepared and further screened to identify the variant, which binds to the ligand, thus the variants have to be prepared. The specification has not disclosed which peptides, polynucleotides, carbohydrates, or organic molecules have the 'optimal binding activity', and in absence of teachings in the specification the claimed method cannot be said to have been described adequately.

Response to Arguments

Applicant's arguments filed 11/2/2004 have been fully considered but they are not persuasive. Applicant maintains that the specification provides sufficient description and guidance to convey to one skilled in the art that the applicant was in possession of the claimed invention at the time the application was filed. Applicant argues that in contrast to the Office action's assertion that the claims encompass an infinite number of variations, the claimed population of variant ligands are related by structure and function. Applicant argues that although a working example is not required, the specification provides a working example applicable to ligand variants in Example V of antibody variant receptors and anti-idiotypic antibodies. Applicant's representative is not aware of any precedent for the assertion that the more unpredictable the art, the

greater the showing required for both enablement and adequate disclosure, and requests the relevant authority.

Applicant's traversal is not deemed persuasive because the claims are drawn to the genera of ligands and variant ligands and receptors, and the specification does not provide a sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See Regents of the University of California v. Eli Lilly, 119 F.3d, 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998); and MPEP 2163. "A 'representative number of species' means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. The disclosure of only one species encompassed within a genus adequately describes a claim directed to that genus only if the disclosure 'indicates that the patentee has invented species sufficient to constitute the gen[us].' See Enzo Biochem, 323 F.3d at 966, 63 USPQ2d at 1615; Noelle v. Lederman, 355 F.3d 1343, 1350, 69 USPQ2d 1508, 1514 (Fed. Cir. 2004) (Fed. Cir. 2004) ('[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species

because there may be *unpredictability* in the results obtained from species other than those specifically enumerated.'" [Emphasis added]). MPEP 2163.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

14. Claims 10-18 and 39-41, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 39 and 41 are vague and indefinite for reciting language for determining binding of a ligand to a receptor by contacting a collective ligand variant population with a population of five or more receptors or one or more receptors. The claimed method is either missing a method step or the method is intended to identify the entire population of ligand variants or a library of ligands which bind to a ligand. Applicants are requested to clarify.

Claims 11 and 18 recite "'further comprising dividing said collective ligand variant population into two or more sub-populations . . . and detecting one or more ligand variant subpopulations'; it is not clear whether applicants mean that claims 11 and 18 are methods for determining binding of a ligand or one or more ligand variant subpopulations. Applicants are requested to clarify.

Claim 14 is vague and indefinite for reciting 'optimal binding activity', which is a relative term. The specification disclosure of the term has various different meanings,

and none would read on the instant claimed limitations. And the specification has not disclosed the 'optimal binding of a ligand variant to a receptor".

Claim 17 recites the language "to tag", in the last line, which instead should probably read as "to a tag".

New Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 10-15, 17, 18, 39-41, and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Sharon, US 5,789,208.

The instant claims briefly recite a method for determining binding of a ligand to a receptor comprising contacting a collective ligand variant population with a population of receptors and detecting binding of a receptor from said population of receptors to a ligand from said collective ligand variant population.

Sharon, US 5,789,208, throughout the patent and abstract, teaches methods for determining binding of a ligand to a receptor, comprising libraries of protein ligands, (which read on the "collective ligand variant populations" of the instant claims) that bind to whole cells and components or extracts thereof, that display antigenic determinants (which read on the "receptors" of the claimed invention). The libraries taught by Sharon

include polyclonal antibodies, receptor proteins and other proteins with variable regions, and nucleic acid vectors used to create antigen-specific polyclonal libraries (col. 8, lines 11-57, as in instant claim 15), antisera to tumor cells (col. 23, lines 60-col. 24, line 3), and Fab phage display libraries (e.g., col. 6, lines 12-27; col. 32 lines 15-53, Example 10). Sharon states that an antibody library targets many different epitopes and that tumor cells used for immunization present many epitopes to the immune system (col. 33, line 57-col. 34, line 44, Example 12). Sharon at col. 5, lines 27-39, teaches that polyclonal antibodies are directed to many different antigenic determinants (which read on one or more receptors of the claims) on a target cell surface. Sharon at col. 9, lines 52-67, teach that "[d]uring an immune response many thousands of different B cell clones, specific for each antigenic determinant, are generated and proliferate creating a large diversity of antibodies", which indicates that there are many thousands of antigenic determinants (taken to read on the five or more or one or more receptors of the claimed invention) taking part in the ligand receptor pairing. Also Sharon contemplates specific receptor molecules found on surface of cells, including blood cells, lymphocytes and cells of the immune response, particularly major histocompatibility antigens, T cell receptor comprising alpha and beta heterodimers, (Sharon at col. 1, lines 49-61), B cell receptors, including immunoglobulin, natural killer cell receptors, macrophage receptors and parts and combinations thereof and tissues containing extracellular matrix (col. 18, lines 29-41), which indicates populations of five or more receptors, as in the instant claims, because Sharon teaches assaying binding of blood cells with the antibody libraries. Sharon at col. 4, lines 29-31, col. 7, lines 41)

teach tagging antibodies with radioactive isotopes, toxins and drugs (as in claims 17 and 39). Sharon at col. 10, line 1-col. 11, line 16, teach eliciting antibody responses by injecting animals or exposing cells to neoplastic tissue derived from tumor tissues, blood and blood related tissues, biopsied tissues, cancerous tissues, malignant and metastasized tissues, or extracts of neoplastic tissues to obtain a single target antigen, group of antigens or antigen-containing extract. Sharon at col. 14, line 12-col. 15, line 10, teach absorption of antibody libraries or sublibraries (reading on subpopulations of collective ligand variant populations, as in instant claims 11 and 18), against neoplastic or normal tissue, in order to select binding antibodies. Thus Sharon teaches determining binding of a ligand to a receptor comprising contacting a library of antibodies (reading on a collective ligand variant population) with a population of five or more receptors, or one or more receptors.

16. Claims 10-14, 18, 40, 41, and 43 are rejected under 35 U.S.C. 102(e) as being anticipated by Houghten et al., US 6,287,787.

The instant claims briefly recite a method for determining binding of a ligand to a receptor comprising contacting a collective ligand variant population with a population of receptors and detecting binding of a receptor from said population of receptors to a ligand from said collective ligand variant population.

Houghten et al., throughout the patent and at col. 32, line 30-col. 35, line 19, and col. 35, line 25-col. 40, line 47 teach that a dimeric oligopeptide mixture set and its individual members are ligands in ligand-receptor binding complex formation. Houghten

teaches exemplary receptor molecules that are antibody combining site-containing molecules, such as whole antibodies, F(ab), $F(ab')_2$ and Fv antibody portions, solubilized or non-solubilized cell surface receptor molecules including CD4 receptor, internal cellular receptors, enzymes and viral protein receptors, (which read on the five or more or one or more receptors of the claimed invention). Furthermore, Houghten et al., in the Examples at col. 35, line 25-col. 40, line 47, teach two "sets" of dimeric oligopeptide mixtures" and "sub-group mixtures" that read on the "collective ligand variant populations" and "subpopulations" of the instantly claimed invention. Houghten teach determining binding of the oligopeptide mixtures to monoclonal antibody 17D09, monoclonal antibody HyHEL-5, trypsin inhibitors, opioid receptors

Conclusion

17. Claims 10-18 and 39-41, and 43 are rejected.

18. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Lerner et al., US 5,462,856.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

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PADMASHRI PONNALURI
PRIMARY EXAMINER